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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/431,451	11/01/1999	PERIANNAN SENAPATHY	34623.005	8738

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INTELLECTUAL PROPERTY DEPARTMENT
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EXAMINER	
SISSON, BRADLEY L	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 11/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/431,451	SENAPATHY, PERIANNAN	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communicati n app ars on the cover sheet with the corr spondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10-12,14-26,28 and 29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10-12,14-26,28 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 15 September 2003 has been entered.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 1-8 10-12, 14-26, 28 and 29 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over US Patent 5,807,679 (Kamb).

6. For convenience, claims 1, 12, and 19, the only independent claims, are reproduced below.

1. **[AMENDED FOUR TIMES] A method of amplifying desired regions of nucleic acid from a nucleic acid template comprising:**
   - **(a) providing a plurality of first PCR primers, each first primer having an overall length of from about 10 nucleotides to about 30 nucleotides and further having a region of fixed nucleotide sequence identical or complementary to a consensus sequence of interest and a region of randomized nucleotide sequence located 5' to, 3' to, or flanking the region of fixed nucleotide sequence;**
   - **(b) providing a plurality of second PCR primers, each second primer having an overall length of from about 10 nucleotides to about 30 nucleotides and further having a region of arbitrary, yet fixed nucleotide sequence and a region of randomized nucleotide sequence located 5' to, 3' to, or flanking the region of fixed nucleotide sequence; and then**
   - **(c) amplifying the nucleic acid template via the PCR using the plurality of first PCR primers and the plurality of second PCR primers under conditions wherein a subset of the plurality first primers binds to the consensus sequence of interest substantially wherever it occurs in the template, and a subset of the plurality of second primers binds to the template at locations removed from the first primers such that nucleic acid regions flanked by the first primer and the second primer are specifically amplified.**

12. **[AMENDED FOUR TIMES]** A method of amplifying exons from a nucleic acid template comprising:
   (a) providing a plurality of first PCR primers, each first primer having an overall length of from about 10 nucleotides to about 30 nucleotides and further having a region of fixed nucleotide sequence identical or complementary to a consensus sequence of a 3' splice region and a region of randomized nucleotide sequence located 5' to, 3' to, or flanking the region of fixed nucleotide sequence;
   (b) providing a plurality of second PCR primers, each second primer having an overall length of from about 10 nucleotides to about 30 nucleotides and further having a region of fixed nucleotide sequence reversely complementary to a consensus sequence of a 5' splice region and a region of randomized nucleotide sequence located 5' to, 3' to, or flanking the region of fixed nucleotide sequence; and then
   (c) amplifying the nucleic acid template via the PCR using the plurality of first PCR primers and the plurality of second PCR primers under conditions wherein a subset of the plurality first primers binds to a sequence reversely complementary to the 3' splice consensus sequence substantially wherever it occurs in the template, and a subset of the plurality of second primers binds to the 5' splice consensus sequence substantially wherever it occurs in the template, such that exons flanked by the first primer and the second primer are specifically amplified.

19. **[AMENDED FOUR TIMES]** A method of amplifying regions flanking a consensus sequence in a nucleic acid template of totally or partially unknown sequence comprising:
   (a) providing a plurality of first PCR primers, each first primer having an overall length of from about 10 nucleotides to about 30 nucleotides and further having a region of fixed nucleotide sequence identical or complementary to a consensus sequence of interest and a region of randomized nucleotide sequence located 5' to, 3' to, or flanking the region of fixed nucleotide sequence;
   (b) providing a plurality of second PCR primers, each second primer having an overall length of from about 10 nucleotides to about 30 nucleotides and further having a region of arbitrary, yet fixed nucleotide sequence and a region of randomized nucleotide sequence located 5' to, 3' to, or flanking the region of fixed nucleotide sequence; then
   (c) amplifying the nucleic acid template via the PCR using the plurality of first PCR primers and the plurality of second PCR primers under conditions wherein a subset of the plurality first primers binds to the consensus sequence of interest substantially wherever it occurs in the template, and a subset of the plurality of second primers binds to the template at locations removed from the first primers such that nucleic acid regions flanked by the first primer and the second primer are specifically amplified; then
   (d) incorporating the amplified nucleic acid of step (c) into a library;
   (e) sequencing a portion of amplified nucleic acid from a particular clone from the library of step (d) and providing a third PCR primer of unique sequence and having an overall length of at least about 10 nucleotides which will prime PCR amplification from the sequenced portion of DNA;

(f) providing a plurality of fourth PCR primers, each fourth primer having an overall length of at least about 10 nucleotides and further having a region of arbitrary, yet fixed nucleotide sequence and a region of randomized nucleotide sequence located 5' to, 3' to, or flanking the region of fixed nucleotide sequence; and then

(g) amplifying the nucleic acid present in the template via the PCR using the third PCR primer and the plurality of fourth PCR primers under conditions wherein the third primer binds to the sequenced portion of nucleic acid from step (e), and a subset of the plurality of fourth primers binds to the template at locations removed from the third primers such that nucleic acid regions flanked by the third primer and the fourth primer are specifically amplified.

7. As seen above, the claimed method requires

providing a plurality of first PCR primers, each first primer having an overall length of from about 10 nucleotides to about 30 nucleotides and further having

Kamb, column 3, discloses performing polymerase chain reaction (PCR). Column 6, lines 56-61, discloses "it is preferable to use primers of lengths 13-30 nucleotides, more preferably primers of lengths 15-25, and most preferably primers of 15-20 nucleotides." Accordingly, the limitation of length is fairly taught by the prior art of record.

8. The claimed methods require the primers to comprise

a region of fixed nucleotide sequence identical or complementary to a consensus sequence of interest and a region of randomized nucleotide sequence located 5' to, 3' to, or flanking the region of fixed nucleotide sequence;

Kamb, column 3, lines 25-26, teaches that his primers "have unique sequences at their 5' ends and degenerate sequences at their 3' ends' are used. Also disclosed is the use of pools of primers. The "unique sequence" is considered to meet the limitation that the primers contain a sequence complementary to the sequence of interest. Kamb, column 3, where it is disclosed that there is a "degenerate sequence at their 3' ends", meets the limitation that the primers also comprise "a region of randomized nucleotide sequence".

Claim 19 requires:

amplifying the nucleic acid present in the template via the PCR using the third PCR primer and the plurality of fourth PCR primers under conditions wherein the third primer binds to the sequenced portion of nucleic acid from step (e), and a subset of the plurality of fourth primers binds to the template at locations removed from the third primers such that nucleic acid regions flanked by the third primer and the fourth primer are specifically amplified.

Kamb, column 8, teaches use of multiple primers pairs , including use of a third and fourth primer, such that multiple nucleic acids of interest are amplified.

9. Kamb, column 3, teaches that "the present invention takes advantage of combining in parallel the power of PCR techniques to increase dramatically the rate of completely sequencing very large fragments of DNA."

10. Column 6 discloses performing PCR on host DNA that is part of a vector. Column 6 further teaches "[a]ny standard PCR condition can be used." Such a disclosure is considered to meet the limitation of amplifying genomic eukaryotic and prokaryotic sequences as well as amplifying RNA. Column 1, penultimate paragraph, states that RNA template can be sued where one wishes to amplify only exons. The above disclosures are considered to meet the limitation that genomic, chromosomal, and subchromosomal regions can be amplified.

11. The aspect of performing an amplification reaction with said plurality of primers is considered to meet the limitation of generating members of a library and that the amplicons are added to the library.

12. Column 1 discloses that research is being conducted into sequencing the genomes of bacteria (prokaryotes), viruses, and humans.

13. The aspect of amplifying nucleic acids that have greater than 50%, less than 50% or 50% G:C content (claims 14 and 28) is considered to fairly encompass all nucleic acids and as such, the nucleic acids amplified by Kamb have as an inherent property just such a G:C content.

14. For the above reasons and in the absence of convincing evidence to the contrary, the invention of claims 1-8, 10-12, 14-26, 28, and 29 are deemed anticipated by the teachings of Kamb, and are therefore rejected under 35 USC 102(b). In the event that Kamb does not anticipate the claimed invention, such disclosure is deemed to render the claimed invention obvious and are rejected under 35 USC 103(a).

Response to argument

15. At page 3 of the response received 15 September 2003 (hereinafter the response), it is asserted that Kamb does not anticipate the claimed invention as the prior art does not teach or suggest having primers that include "a region of fixed sequence that is 'identical to or complementary to' a consensus sequence of interest." This argument has been fully considered and has not been found persuasive. Kamb, column 3, lines 25-26, teaches that his primers "have unique sequences at their 5' ends and degenerate sequences at their 3' ends' are used. The "unique sequence" is considered to meet the limitation that the primers contain a sequence complementary to the sequence of interest. Kamb, column 3, where it is disclosed that there is a "degenerate sequence at their 3' ends", meets the limitation that the primers also comprise "a region of randomized nucleotide sequence". The fact that the primers are identical o complementary to the sequence of interest is evidenced by the amplification of the sequence of interest.

16. Applicant, page 3 of the response, asserts that the claimed invention is further distinguished over the prior art as a second set of primers are required, and these primers also are required to have an arbitrary region of fixed sequence and a randomized region. The preceding

argument has been fully considered and has not been found persuasive. While Kamb does disclose performing PCR with individualized primer pairs, Kamb directs attention to performing PCR with multiple sets of primers that have been combined or "pooled." It is because of this pooling feature/concept that the power of performing PCR in parallel can be achieved. Accordingly, the prior art fairly teaches this limitation.

17. Applicant, page 3, asserts that the primers of Kamb bind in a random manner and that "there is no attempt by Kamb to specifically amplify any distinct portion of the template that was selected in advance." This argument has been fully considered persuasive and has not been found persuasive towards the withdrawal of the rejection for as shown above, the primers of Kamb do result in the amplification of desired sequences. Further, there is no limitation in the claimed method that precludes the presence of additional primers that do not bind to the sequence of interest. As for the claimed method requiring the amplification of known sequences, it is noted that the method of claim 19 seeks to amplify "a nucleic acid sequence template of totally ...unknown sequence." Accordingly, and in the absence of convincing evidence to the contrary, claims 1-8, 10-12, 14-26, 28, and 29 are deemed anticipated by the teachings of Kamb, and are therefore rejected under 35 USC 102(b) or in the alternative, are rejected under 35 USC 103(a).

Conclusion

18. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under

37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

19. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (703) 308-3978. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

21. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

22. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

B. L. Sisson

Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
07 November 2003